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DATE: Monday, April 10, 2006

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		<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ</i>	
<input type="checkbox"/>	L5	L4 same l2	19
<input type="checkbox"/>	L4	(HMGB\$ or HMG\$) adj (anti or antibod\$ or mab)	45
<input type="checkbox"/>	L3	l2 same inflammation	161
<input type="checkbox"/>	L2	(HMGB\$ or HMG\$) same cytokine	430
<input type="checkbox"/>	L1	Newman-walter.in.	61

END OF SEARCH HISTORY

ACCESSION NUMBER: 1999:74851 LIFESCI

TITLE: HMG-1 as a late mediator of endotoxin lethality in mice

AUTHOR: Wang, H.; Bloom, O.; Zhang, Minghuang; Vishnubhakat, J.M.;
Ombrellino, M.; Che, Jiantu; Frazier, A.; Yang, H.;
Ivanova, S.; Borovikova, L.; Manogue, K.R.; Faist, E.;
Abraham, E.; Tracey, K.J.; et al.

CORPORATE SOURCE: Dep. Emerg. Med., North Shore Univ. Hosp.-New York Univ.
Sch. Med., Manhasset, NY 11030, USA; E-mail:
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SOURCE: Science (Washington) [Science (Wash.)], (19990709) vol.
285, no. 5425, pp. 248-251.
ISSN: 0036-8075.

DOCUMENT TYPE: Journal

FILE SEGMENT: F; J; X; N

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Endotoxin, a constituent of Gram-negative bacteria, stimulates macrophages to release large quantities of tumor necrosis factor (TNF) and interleukin-1 (IL-1), which can precipitate tissue injury and lethal shock (endotoxemia). Antagonists of TNF and IL-1 have shown limited efficacy in clinical trials, possibly because these cytokines are early mediators in pathogenesis. Here a potential late mediator of lethality is identified and characterized in a mouse model. High mobility group-1 (HMG-1) protein was found to be released by cultured macrophages more than 8 hours after stimulation with endotoxin, TNF, or IL-1. Mice showed increased serum levels of HMG-1 from 8 to 32 hours after endotoxin exposure. Delayed administration of antibodies to HMG-1 attenuated endotoxin lethality in mice, and administration of HMG-1 itself was lethal. Septic patients who succumbed to infection had increased serum HMG-1 levels, suggesting that this protein warrants investigation as a therapeutic target.

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ACCESSION NUMBER: 1999:29382808 BIOTECHNO
TITLE: Proinflammatory cytokines (tumor necrosis factor and interleukin 1) stimulate release of high mobility group protein-1 by pituicytes
AUTHOR: Wang H.; Vishnubhakat J.M.; Bloom O.; Zhang M.; Ombrellino M.; Sama A.; Tracey K.J.
CORPORATE SOURCE: Dr. H. Wang, North Shore University Hospital, New York Univ. School of Medicine, Picower Inst. for Medical Research, 350 Community Dr, Manhasset, NY 11030, United States.
SOURCE: Surgery, (1999), 126/2 (389-392), 13 reference(s)
CODEN: SURGAZ ISSN: 0039-6060
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background. Cytokines mediate the metabolic and physiologic responses to injury and infection. Anterior pituitary cells express receptors for tumor necrosis factor (TNF) and interleukin 1 (IL-1), which can signal these cells to release corticotropin, growth hormone, and cytokines such as IL-1 and macrophage migration inhibitory factor. This interaction provides an important link between the immune system and the neuroendocrine system. We reasoned that pituicytes activated with TNF or IL-1 might release previously unrecognized factors that could participate in this signaling from the neuroendocrine to the immune system. Methods. Proteins released from rat pituicytes (GH.sub.3) after stimulation with proinflammatory cytokines were identified by N-terminal amino acid sequencing. Polyclonal antibodies against a peptide corresponding to the N-terminal amino acid sequence were generated and used to determine the kinetics of protein release. Results. Cytokine stimulation induced the release of a 30-kd protein from rat pituicytes. After the protein was isolated and the N-terminal amino acid sequence determined, a protein database analysis revealed that it is high mobility group-1 (HMG-1) protein. TNF and IL-1 induced the release of HMG-1 from pituicytes in a time- and dose-dependent manner. Interferon gamma alone did not induce the release of HMG-1, but it enhanced TNF-induced HMG-1 release. Conclusion. Stimulation of pituicytes by TNF or IL-1 induces the release of HMG-1, which may participate in the regulation of neuroendocrine and immune responses to infection or injury.

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ACCESSION NUMBER: 1999:13443 PHIN
DOCUMENT NUMBER: S00630876
DATA ENTRY DATE: 23 Jul 1999
TITLE: Possible new target for septic shock
SOURCE: Scrip (1999) No. 2457 p22
DOCUMENT TYPE: Newsletter
FILE SEGMENT: FULL

TX The scientists, from the US, Germany and Sweden, say that these clinical trials may have failed because cytokines such as TNF are early mediators in the pathogenesis of shock. They have now characterised a late mediator of shock, known as high mobility group-1 protein (HMG-1), which they found to be released by macrophages in culture eight hours after stimulation with endotoxin. In mice models of shock, the administration of antibodies to HMG-1 attenuated endotoxin death, while the protein itself was lethal (Science, July 9th, p 248).

ACCESSION NUMBER: 2000:30728141 BIOTECHNO
TITLE: Cutting edge: HMG-1 as a mediator of acute lung
inflammation
AUTHOR: Abraham E.; Arcaroli J.; Carmody A.; Wang H.; Tracey
K.J.
CORPORATE SOURCE: Dr. E. Abraham, Div. Pulmon. Sci./Critical Care Med.,
Univ. of Colorado Hlth. Sci. Center, Box C272, 4200
East Ninth Avenue, Denver, CO 80262, United States.
E-mail: edward.abraham@uchsc.edu
SOURCE: Journal of Immunology, (15 SEP 2000), 165/6
(2950-2954), 25 reference(s)
CODEN: JOIMA3 ISSN: 0022-1767
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Acute inflammatory lung injury is often a delayed complication of
critical illness and is associated with increased mortality. High
mobility group-1 (HMG-1) protein, in addition to its role as a
transcriptional regulatory factor, has recently been identified as a late
mediator of endotoxin lethality. In the present studies, HMG-1
given intratracheally produced acute inflammatory injury to the lungs,
with neutrophil accumulation, the development of lung edema, and
increased pulmonary production of IL-1 β , TNF- α , and
macrophage-inflammatory protein-2. In endotoxin-induced acute lung
inflammation, administration of anti-HMG-1 Abs either
before or after endotoxin exposure decreased the migration of neutrophils
to the lungs as well as lung edema. These protective effects of
anti-HMG-1 were specific, because pulmonary levels of
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ACCESSION NUMBER: 2001254670 ESBIODBASE
TITLE: Dual roles for HMGB1: DNA binding and cytokine
AUTHOR: Czura C.J.; Wang H.; Tracey K.J.
CORPORATE SOURCE: Dr. K.J. Tracey, Center for Patient-Oriented Research,
Laboratory of Biomedical Science, North Shore/LIJ
Research Institute, 350 Community Drive, Manhasset, NY
11030, United States.
E-mail: kjtracey@sprynet.com
SOURCE: Journal of Endotoxin Research, (2001), 7/4 (315-321),
79 reference(s)
CODEN: JENREB ISSN: 0968-0519
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English

- AB Effective therapies against overwhelming Gram-negative bacteremia, or sepsis, have eluded successful development. The discovery that tumor necrosis factor (TNF), a host-derived inflammatory mediator, was both necessary and sufficient to recapitulate Gram-negative sepsis raised cautious optimism for developing a targeted therapeutic. However, the rapid kinetics of the TNF response to infection defined an extremely narrow window of opportunity during which anti-TNF therapeutics could be successfully administered. HMGB1 was previously studied as a DNA-binding protein involved in DNA replication, repair, and transcription; and as a membrane-associated protein that mediates neurite outgrowth. A decade-long search has culminated in our identification of HMGB1 as a late mediator of endotoxemia. HMGB1 is released by macrophages upon exposure to endotoxin, activates many other pro-inflammatory mediators, and is lethal to otherwise healthy animals. Elevated levels of HMGB1 are observed in the serum of patients with sepsis, and the highest levels were found in those patients that died. The delayed kinetics of HMGB1 release indicate that it may be useful to target this toxic cytokine in the development of future therapies.
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CORPORATE SOURCE: Dr. K.J. Tracey, Center for Patient-Oriented Research,
Laboratory of Biomedical Science, North Shore/LIJ
Research Institute, 350 Community Drive, Manhasset, NY
11030, United States.
E-mail: kjtracey@sprynet.com
SOURCE: Journal of Endotoxin Research, (2001), 7/4 (315-321),
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